## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. The amendments filed on Oct. 26, 2009 have been entered.

### *Status of the Claims*

Claims 1, 3, 4, 7, and 9-20 are pending. Claims 1, 12, and 13 have been amended; claims 2, 5, 6, and 8 are cancelled; claims 14-20 have been added. Claims 1, 3, 4, 7, and 9-20 are now under consideration. This Office Action is in response to the request for continued examination filed on Oct. 26, 2009.

### *Information Disclosure Statement*

References lined-through on the information disclosure statement(s) were not considered because they were not provided in English.

### *OBJECTIONS/REJECTIONS WITHDRAWN*

The rejections of claims 1, 3, 4, 7, and 9-13 under 35 U.S.C. 103(a) of record in the prior Office Actions are withdrawn in light of the claim amendments.

***OBJECTIONS/REJECTIONS MAINTAINED***

The rejection of claims 1, 3, 4, 7, and 9-13 under 35 U.S.C. 112, 1st paragraph, lack of written description, is maintained as discussed below.

The rejection of claims 1, 3, 4, 7, and 9-13 under 35 U.S.C. 112, 2nd paragraph is maintained, as discussed below.

***Claim Rejections - 35 USC § 112 (1st Paragraph) (Maintained)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 1, 3, 4, 7, and 9-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The response filed Oct. 28, 2008 (and maintained in the claims filed Oct. 26, 2009) has introduced NEW MATTER into the claims. Amended claims 1, 7, and 9 recite the broad genus of salt(s) of the claimed active compounds. Support in the instant application is found for *acid addition* salts of the claimed active compounds. However, written description support is lacking for the broader genus of all salts thereof,

as is instantly claimed. In the absence of support for *all* salts of the claimed compounds, the recitations, "...salts thereof" (claim 1), "...a salt of this compound" (claim 7), and "...a salt thereof" (claim 9) are new matter and must be removed from the claims.

The response did not point out where support for amended claims 1 and 9 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). Instant claims 1, 7, and 9 now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in amended claims 1, 7, and 9, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claims 1, 7, and 9 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

***Response to Arguments***

Applicants' arguments have been fully considered but are not persuasive. In the response of May 26, 2009, applicants argue that the recitation "derivatives thereof"

provides proper support for ALL salt forms of the compounds recited in claims 1, 7, and 9 (see p. 5 of the response dated 5/26/09).

It is well established that a genus does not anticipate a species. While written description does not require *ipsis verbis* support, no support exists in the specification for the broad category of all salts. Applicants are arguing that the broad genus of "dereivatives thereof" (which, as established in the Office Action of 5/28/08, itself lacks written description support) provides specific support for the subgenus of all salts, which is not the case. As stated in the Office Action dated Jan. 23, 2009, support is found for the subgenus of acid addition salts, but not the broad genus of ALL salts (which includes, for example, addition salts of bases as well as acids).

***Claim Rejections - 35 USC § 112 (2nd Paragraph)***

**Claims 1, 3, 4, 7, and 9-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

The recitation, "and salts thereof" in the last line of claim 1 renders the claims indefinite. It is unclear whether this recitation is intended to refer to all the compounds in the Markush group, or only to the last compound, which immediately precedes the limitation. Thus, the metes and bounds of the claims are unclear.

***Response to Arguments***

Applicants' arguments have been fully considered but are not persuasive. Applicants argue that the response to the 112 1st paragraph rejection applies to the 112

2nd paragraph rejection (see p. 6 of the response dated 5/26/09).

Applicants' argument regarding the 112 1st paragraph rejection has little relevance to the 112 2nd paragraph rejection since a different problem with the claims is at issue. The issue with the claims under 112 2nd involves a situation where the ordinary artisan could construe the claim in multiple ways (i.e. where the phrase "and salts thereof" could be applied to all of the elements of the Markush group, or alternatively, only to the last of these). The skill of the ordinary artisan would not allow the artisan to surely know which of these options was intended by applicant given the unclear claim construction. The metes and bounds of the claim are indefinite.

## *NEW GROUNDS OF OBJECTION/REJECTION*

### *Claim Rejections - 35 USC § 112 (1st Paragraph)*

**Claims 1, 3, 4, 7, and 9-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The response filed Oct. 26, 2009 has introduced NEW MATTER into the claims. Amended claim(s) 1 and 15 recite that phosphatidylcholine comprises at least 80% by weight of the administration form. There is no support for this limitation in the specification or claims as filed. The only support for any limitation regarding 80%

appears in original claim 2. However, this limitation occurs in the context of a "phosphatidylcholine fraction", which, as established in the prior Office Actions, is not limited to phosphatidylcholine. A "phosphatidylcholine fraction" can include other substances in addition to phosphatidylcholine. Thus, there is no nexus between the originally disclosed "phosphatidylcholine fraction" previously claimed and the amount of phosphatidylcholine instantly claimed. In the absence of clear support for the "phosphatidylcholine fraction" being equivalent to the total amount of phosphatidylcholine in the dosage form, the limitation "...wherein the administration form comprises at least 80% by weight of phosphatidylcholine" in claims 1 and 15 is new matter and must be removed from the claims.

The response did not point out where support for the amended claim could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). Instant claims 1 and 15 now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in amended claim 1 and 15, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support

for the limitations recited in present claim 1 and 15 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

***Claim Rejections - 35 USC § 112 (2nd Paragraph)***

**Claims 1, 3, 4, 7, and 9-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Claims 1, 3, 4, 7, and 9-20 are indefinite in the recitation "where appropriate" in claims 1 and 15. It is unclear what conditions qualify as "appropriate". This term is not defined in the instant application and no further guidance is presented. Thus, one of skill in the art would not be apprised of the scope of the claims. The metes and bounds of the claims are unclear.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1, 4, 11, ,12, 14, 15, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over FUJII (M. Fujii, *et al.* (1988) Chem. Pharm. Bull.; 36(6); 2186-2192) in view of SCHNEEWEIS (A. Schneeweis *et al.* (2000) Int. J. Pharm.; 196; 193-196), ENGSTROM (U.S. 5,151,272; Issued Sep. 29, 1992) and SERRA (Serra, S. *et al.* Eur. J. Pharmacol. 2001 November; 430(2-3):369-371; of record) as evidenced by Witepsol W35.**

1. Fujii teaches solid dispersions for the delivery of drugs, particularly poorly water soluble drugs (title; abstract). Fujii teaches that solid dispersions improve the solubilities of poorly water soluble drugs (p. 2186, 1st sentence; last par. of Conclusion). Fujii teaches that phosphatidylcholine (PC) is hydrophilic, interacts with some drugs in water, and is useful as a carrier for solid dispersions of drugs (p. 2186, 1st sentence of 2nd par.). Fujii teaches that PC can be easily oxidized because of its unsaturated acyl

chains. Thus, the PC used by Fujii is hydrogenated and is composed of only stearic acid and palmitic acid fatty acid chains (p. 2186, 2nd par.; p. 2187 under Materials). Both stearic and palmitic acids are saturated. Thus, it is clear that the PC used by Fujii is completely saturated (i.e. more than 90% saturated). Fujii teaches that the solid dispersion is prepared as a glassy film (i.e. is planiform) (p. 2187, 3rd par. under Preparation of IM-PC; p. 2190, 1st par. under Preparation and Physiochemical Properties of FP-PC and KP-PC; Fig. 4). Fujii teaches that the solubilities of the drugs tested were 1.5-5 times those of comparable powder preparations (p. 2192, Conclusion). Thus, Fujii teaches each and every limitation of claim 1 except for the specific drugs recited. However, it is well within the purview of the skilled artisan to replace a drug in a given formulation with another drug known to be useful for treating a different condition, especially if the formulations are similar to one another. Any medicinal chemist reading Fujii would immediately envisage using other drugs in the formulation disclosed based on the disease/patient to be treated. Applicants are advised that the, recitation of a particular drug, without more, will generally not patentably distinguish over the prior art. It is also well-within the skill of the artisan to use a known dosage form in its intended mode of use.

2. For example, Schneeweis teaches a drug delivery system for mucosal delivery comprising a solid-reversed-micellar-solution (SRMS) (title; abstract). Schneeweis' compositions are comprised of a drug in a lipid carrier that is 70% hardened fat (i.e. Witepsol W35, which is a mixture of hydrogenated glycerides, see evidentiary reference) and 30% lecithin (p. 193, 2nd col.). The lecithin is at least 90%

phosphatidylcholine (p. 194, under section 2.1). Schneeweis teaches that these dosage forms exhibit nearly zero order kinetics for release of the drug (Fig. 1). It is noted that Fujii's compositions also display close to zero order kinetics (Fig. 4). Thus, both Fujii and Schneeweis teach drug delivery compositions having a lipid carrier (both containing PC) and having similar drug release properties. Schneeweis teaches that on contact with water, the dosage form transforms into a system of lamellar liquid crystals (mesophase), this form being responsible for the extended drug release (p. 193, 2nd col.; p. 194, 1st full par.; p. 195, last par. under section 3.1).

3. Furthermore, Engstrom discloses controlled release preparations comprising liquid crystalline forming amphiphile and a drug for oral, rectal, and transdermal drug delivery (abstract; col. 4, lines 21-24). Engstrom teaches that an increasing amount of amphiphile in water sequentially gives rise to micellar, cubic, hexagonal, and lamellar phases, the structures of which are well-known (col. 1, lines 23-26). Engstrom teaches that all of these phases have the possibility to solubilize or disperse both water-soluble and water insoluble compounds (col. 1, item b)). Engstrom also teaches that the occurrence of these phases is not restricted to specific amphiphiles (col. 1, lines 59-60). Engstrom teaches that these liquid crystalline phases are interesting candidates for matrices in controlled release preparations, the most important feature being the possibility to dissolve both water-soluble and water insoluble compounds in the phases due to their amphiphilic character. Moreover, the highly ordered structures with distinct hydrophilic and hydrophobic domains put restrictions on the diffusion of added compounds, a fact which may be advantageously used for controlled-release purposes

(col. 1, line 66 to col. 2, line 8). In light of these teachings, the skilled artisan would have a high expectation that the compositions of Fujii would form lamellar mesophases upon contact with water. This is true because the highly related compositions of Schneeweis are known to form these phases, and because Engstrom teaches that such phases are formed by almost any amphiphile in water at sufficient concentration. This analysis is further supported by the evidence provided by applicants illustrating the formation of lamellar structures (see http://barrett-group.mcgill.ca/teaching/liquid_crystal/LCOS.htm; pages 1 and 2).

4. Fujii teaches the solid pharmaceutical administration form as discussed above. However, SR 141716 is not disclosed. As stated above, the skilled artisan would immediately envisage using other drugs in the formulation disclosed based on the disease/patient to be treated, particularly since Fujii is a proof-of-concept type study and not intended to be limited to the three NSAIDs studied. Also, Engstrom makes it clear that amphiphilic drug carriers are applicable to both water-soluble and water insoluble drugs. Serra teaches that SR 141716, a low solubility drug is useful in the treatment of alcohol addiction (abstract). Thus, if an artisan wanted to prepare a mucosal delivery form for the treatment of alcohol addiction, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use SR 141716 the invention of Fujii. Claims 1, 4, 11, 12, 14, 15, and 20 are obvious over Fujii, Schneeweis, Engstrom, and Serra.

**Claims 3, 13, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujii in view of Schneeweis, Engstrom, and Serra as evidenced**

**by Witepsol W35 as applied to claims 1, 4, 11, ,12, 14, 15, and 20 above, and further in view of MAJETI (U.S. 5,599,554, Issued Feb. 4, 1997; of record).**

5. The teachings of Fujii, Schneeweis, Engstrom, and Serra are presented *supra*. Fujii teaches that water-soluble polymers such as polyethylene glycol or polyvinylpyrrolidone have been used as carriers for solid dispersions of drugs (p. 2186, 1st par.). However, Fujii does not explicitly teach the use of polyvinylpyrrolidone or a maleic acid/alkyl vinyl ether copolymer.

6. Majeti discloses a transmucosally administrable composition for the treatment of addiction (e.g. nicotine craving or smoking withdrawal) (abstract). Majeti teaches that both polyvinylpyrrolidone and alkyl or polyvinyl ether-maleic acid copolymers are suitable polymers to include in the transmucosal composition to create a mucoadhesive film (col. 4, lines 59-64). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include an either polyvinyl pyrrolidone or an alkyl vinyl ether-maleic acid copolymer in the compositions of Fujii, to provide an administration form with satisfactory mucoadhesive properties as taught by Majeti. Claims 3, 13, and 16 are obvious over the prior art.

**Claims 1, 7, 15, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujii in view of Schneeweis, and Engstrom, as evidenced by Witepsol W35 as applied to claims 1, 4, 11, 12, 14, 15, and 20 above, and further in view of ZHANG (U.S. 6,264,981; Issued July 24, 2001) and SHEN (U.S. 6,255,490; Issued July 3, 2001; of record).**

7. The teachings of Fujii, Schneeweis, and Engstrom are presented *supra*. Fujii teaches three NSAIDs as model compounds to illustrate the drug delivery potential of the dosage forms, but do not teach the drugs instantly claimed.

8. However, any medicinal chemist reading Fujii would immediately envisage using other drugs in the formulation disclosed based on the disease/patient to be treated. For example, Zhang discloses an oral transmucosal drug formulation comprising a pharmaceutical agent in solid solution with a dissolution agent (abstract; col. 5, lines 40-51; col. 6, lines 31-33) and disclose lecithin as one of the acceptable dissolution agents (col. 7, line 29). Zhang teaches that the pharmaceutical agent of their invention may be any drug substance used for, *inter alia*, prevention, control, or treatment of a condition. Zhang further teaches that the dosage form can be used with "a variety of drugs affecting the central nervous system" including naloxone (col. 9, lines 39-53), which is well known to be useful in treating opioid addiction.

9. Shen discloses epibatidine in addition to a wide variety of similar compounds, some of which are useful in the treatment of cognitive, neurological, and mental disorders and disorders characterized by altered cholinergic function (i.e. addiction) (col. 7, lines 58-63). Thus, if an artisan wanted to prepare a mucosal delivery form for the treatment of cognitive, neurological, and mental disorders, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a known anti-addictive cholinergic receptor agonist (i.e. epibatidine) as the active compound in the invention of Fujii. Claims 1, 7, 15, and 17 are obvious over the prior art.

**Claims 1, 9, 15, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujii in view of Schneeweis, and Engstrom, as evidenced by Witepsol W35 as applied to claims 1, 4, 11, 12, 14, 15, and 20 above, and further in view of Zhang and CARY (U.S. 6,197,827; Issued March 6, 2001; of record).**

10. The teachings of Fujii, Schneeweis, Engstrom, and Zhang are presented *supra*. Fujii teaches three NSAIDs as model compounds to illustrate the drug delivery potential of the dosage forms, but do not teach the drugs instantly claimed. Zhang teaches that a wide variety of drugs, including anti-addictives, are useful in tansmucosal dosage forms as discussed above.

11. Cary discloses both mecamylamine and bupropion as useful agents in smoking cessation therapy and treatment of cocaine addiction (abstract). Thus, if an artisan wanted to prepare a mucosal delivery form for smoking cessation, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a known anti-addictive drug (i.e. mecamylamine or bupropion) as the active compound in the invention of Fujii. Claims 1, 9, 15, and 18 are obvious over the prior art.

**Claims 1, 10, 15, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujii in view of Schneeweis, and Engstrom, as evidenced by Witepsol W35 as applied to claims 1, 4, 11, 12, 14, 15, and 20 above, and further in view of Zhang and PLOTNIKOFF (U.S. 3,706,831; Issued December 19, 1972; of record).**

12. The teachings of Fujii, Schneeweis, Engstrom, and Zhang are presented *supra*. Fujii teaches three NSAIDs as model compounds to illustrate the drug delivery potential of the dosage forms, but do not teach the drugs instantly claimed. Zhang teaches that a wide variety of drugs, including anti-addictives, are useful in tansmucosal dosage forms as discussed above.

13. Plotnikoff discloses disclose various oxazolidinones as useful agents in the treatment of drug addiction (abstract). Thus, if an artisan wanted to prepare a mucosal delivery form for the treatment of drug addiction, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a known anti-addictive drug (i.e. oxazolidinone) as the active compound in the invention of Fujii. Claims 1, 10, 15, and 19 are obvious over the prior art.

***Conclusion***

Claims 1, 3, 4, 7, and 9-20 are rejected. No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin S. Orwig whose telephone number is (571)270-5869. The examiner can normally be reached Monday-Friday 7:00 am-4:00 pm (with alternate Fridays off). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached Monday-Friday 8:00 am-5:00 pm at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

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